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1: FGFR3 fibroblast growth factor receptor 3 (achondroplasia, thanatophoric dwarfism) [*Homo sapiens*]

GeneID: 2261

updated 08-Jul

Summary

Official Symbol	FGFR3	provided by HG
Official Full Name	fibroblast growth factor receptor 3 (achondroplasia, thanatophoric dwarfism)	provided by HG
Primary source	HGNC:3690	
See related	Ensembl: ENSG00000068078; HPRD:00624; MIM:134934	
Gene type	protein coding	
RefSeq status	REVIEWED	
Organism	<i>Homo sapiens</i>	
Lineage	<i>Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini; Catarrhini; Hominidae; Homo</i>	
Also known as	ACH; CEK2; JTK4; CD333; HSFGR3EX	

Summary The protein encoded by this gene is a member of the fibroblast growth factor receptor family, where amino acid sequence is highly conserved between members and throughout evolution. FGFR family members differ from one another in their ligand affinities and tissue distribution. A full-length representative protein would consist of an extracellular region, composed of three immunoglobulin-like domains, a single hydrophobic membrane-spanning segment and a cytoplasmic tyrosine kinase domain. The extracellular portion of the protein interacts with fibroblast growth factors, setting in motion a cascade of downstream signals, ultimately influencing mitogenesis and differentiation. This particular family member binds acidic and basic fibroblast growth hormone and plays a role in bone development and maintenance. Mutations in this gene lead to craniostylosis and multiple types of skeletal dysplasia. Alternative splicing occurs and additional variants have been described, including those utilizing alternate exon 8 rather than 9, but their full-length nature has not been determined.

Genomic regions, transcripts, and products

Go to reference sequence details

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Genomic context

chromosome: 4; Location: 4p16.3

See FGFR3 in MapV



Bibliography

Related Articles in PubMed

PubMed links

GeneRIFs: Gene References Into Function

1. The technique had a sensitivity and specificity of 100%. CONCLUSION: High resolution melting analysis is a simple, rapid, and sensitive one tube assay genotyping the FGFR3 gene.
2. No sequence variation was found, indicating that mutations in the "hot spot" are not associated with nonsynostotic plagiocephaly.
3. Strong immunohistochemical expression of FGFR3, a superficial staining p... CK20, and a low proliferative activity define those papillary urothelial neopl... low malignant potential that do not recur.
4. Observational study of genotype prevalence and gene-disease association. (Navigator)
5. Observational study of gene-disease association. (HuGE Navigator)
6. Observational study of genetic testing. (HuGE Navigator)
7. FGFR3 mutation frequency was significantly associated with tumor grade.
8. over-expression of FGFR3 protein in many tumours compared to normal bl... and ureteric controls. Increased expression was associated with mutation (... mutant tumours)
9. MM Patients showing the t(4;14) chromosomal translocation at FGFR3 and genes had a significant elevation of serum crosslaps, reported to be the m... most reliably correlated with the extent of bone resorption
10. analysis of FGFR3 mutation in Muenke syndrome
11. a K650Q mutation in the FGFR3 gene may have a role in Acanthosis nigrica [case report]
12. Mutations were detected in 12 of 13 (92.3%) tumor tissues and 11 of 13 (8... urine samples from patients with superficial bladder cancer.
13. The group of low-grade noninvasive papillary tumours is defined by the pre

an FGFR3 mutation

14. FGFR3 mediates hematopoietic transformation by activating RSK2 in a two-fashion, promoting both the ERK-RSK2 interaction and subsequent phosphorylation of RSK2 by ERK.
15. previously undescribed, heterozygous lysine to threonine mutation at codon 1138 of the FGFR3 gene in familial acanthosis nigricans
16. Results suggest that a PLCgamma-STAT1 pathway mediates apoptotic signaling in FGFR3 in genetic dwarfism and chondrogenic cell lines.
17. the mutant S249C FGFR3 may have a role in bladder cancer
18. Mutations are a possible prognostic tool in survival of urothelial carcinoma of the upper urinary tract.
19. FGFR3 may represent a prognostic marker of chromosomally stable bladder cancer with low malignant potential.
20. study showed that FGFR3 mutations appear to be common genetic alterations in multiple seborrheic keratoses with a varying interindividual mutation frequency without specific intraindividual hot spots
21. the fibroblast growth factor family has a pleiotrophic function in human spermatogonia, which physiologically express FGFR3
22. Show preferential occurrence of FGFR3 mutations in seborrheic keratoses of the head and neck. Increased age appears to be a risk factor for these mutations
23. analysis of a Chinese family with autosomal dominant achondroplasia; disease locus was mapped to chromosome 4p16.3, where the FGFR3 gene is located. A novel Ser217Cys mutation in exon 5 of FGFR3 that causes autosomal dominant achondroplasia was identified
24. Although mutation K650M induces defective targeting of receptor, different mechanism characterized by receptor retention at plasma membrane, excessive ubiquitylation and reduced degradation results from mutations of extracellular domain and stop codon.
25. Two patients with clinical and radiological findings of achondroplasia, who have the most common FGFR3 missense mutations.
26. G380R mutation of this gene is common mutation associated with achondroplasia
27. involvement of FGFR-3 in malignant hematopoiesis and FGFR-3 tyrosine kinase in CD34+ leukemic cells
28. data indicate that t(4;14)(p16;q32) and loss of fibroblast growth factor receptor 3 occurred at a very early stage of multiple myeloma and suggest that activation of multiple myeloma SET domain protein may be transforming event of this translocation
29. Nucleotide 1138 in transmembrane domain of FGFR3 gene is the hot point for mutation in ACH and hence its major pathologic cause.

30. FGFR3 expression is significantly associated with two important prognostic stage and grade. Tumours with FGFR3+/p53- phenotype seem to have a distinctive pathway in bladder tumorigenesis.
31. identified a heterozygous missense mutation that is predicted to cause a p. substitution in the tyrosine kinase domain and partial loss of FGFR3 function
32. no evidence that mosaicism for mutations, normally associated with syndromic forms of craniosynostosis, occur in single suture craniosynostosis
33. results indicate that FGFR3 plays a crucial role in the accelerated proliferation of MM carrying t(4;14)(p16.3;q32)
34. introduction of these mutated FGFR3s into ATDC5 cells downregulated PTHrP expression and induced apoptosis with reduction of Bcl-2 expression
35. tumors with FGFR3 mutation appear to have distinctive clinical and biologic characteristics that may help in defining a population of patients for FGFR3 mutation screening
36. results give further support to the fact that the G380R mutation of FGFR3 is the most common mutation causing achondroplasia in different populations
37. These results suggest that constitutive levels of both FGFR1 and FGFR3, but not FGFR4, are essential for FGF-stimulated anchorage-independent growth of C2C12 cells.
38. CHEK2 mutation has a role in hereditary breast cancer
39. Acanthosis nigricans with achondroplasia due to Gly380Arg mutation in FGFR3
40. Reciprocal relationship in gene expression between FGFR1 and FGFR3 in colon tissue plays an important role in the progression of the carcinomas to malignancy
41. Mutations were detected in 23 of 27 (85%) adenoid sebaceous keratoses. FGFR3 mutations were the most frequent mutation type.
42. Identification and characterization of an alternatively spliced isoform
43. Parathyroid hormone receptor type 1/Indian hedgehog expression is preserved in the growth plate of human fetuses affected with activating mutations in the PTHrP receptor protein
44. there is an FGFR3 mutation with a demonstrated deregulatory mechanism involving alternative splicing in the absence of t(4;14) in multiple myeloma patients
45. Cherubism was mapped to region 4p16.3. Because of the associated craniosynostosis, we excluded the FGFR3 gene as a candidate gene for cherubism
46. defective differentiation of chondrocytes is the main cause of longitudinal bone growth retardation in FGFR3-related human chondrodysplasias
47. Differences in spatial patterns of FGFR expression in normal skin may reflect functional diversity in response to FGFs, and in wounded skin FGFs may further promote wound healing via induced FGFRs.

48. A missense mutation in FGFR3 resulted in skeletal dysplasia distinct from thanatophoric dysplasia.
49. FGFR3 is an important cell survival and antiapoptotic factor for multiple myelomas
50. The G370C and S371C mutant receptors spontaneously dimerize in the correct spatial orientation required for effective signal transduction, whereas the 371C mutants, like the WT receptor, may achieve this orientation only on ligand binding
51. Inhibition of FGFR3 in myeloma cell lines was associated with morphologic, phenotypic, and functional changes typical of plasma cell differentiation, including an increase in light-chain secretion and expression of CD31, followed by apoptosis
52. FGFR3IIIS may regulate FGF and FGFR trafficking and function, possibly contributing to the development of a malignant phenotype
53. Overexpression of FGFR3 is associated with urinary tract carcinoma progression
54. Gly380 --> Arg mutation does not alter dimerization energetics of FGFR3 transmembrane domain in detergent micelles or lipid bilayers. This indicates that pathogenesis in achondroplasia cannot be explained simply by higher dimerization of mutant FGFR3.
55. Phosphorylation is essential for FGFR3 ubiquitylation, but is not sufficient to downregulate its internalization-resistant mutants
56. Mutations in bladder cancer previously identified in non-lethal skeletal dysplasias
57. Presence of a Pro250Arg mutation predisposed to an increased transcranial reoperation rate...on the basis of raised intracranial pressure...in apparently "isolated" coronal synostosis
58. Review. The role of FGFR3 in endochondral ossification and mutations leading to achondroplasia are reviewed.
59. First quantitative measurement of mutant receptor tyrosine kinase (RTK) stabilization in the membrane domain environment of FGFR3 shows the precise effect of resultant increase in the dimer fraction on RTK-mediated signal transduction.
60. Results suggest a novel interaction between the SOCS1 and SOCS3 protein with the FGFR3 signaling pathway.
61. PRO-001 antibody is a potent and specific inhibitor of FGFR3 and deserves further study for the treatment of FGFR3-expressing myeloma.
62. MIP-1 alpha promoter function, gene expression, and protein secretion were down-regulated following inhibition of FGFR3 signaling.
63. PIK3CA mutations were strongly associated with FGFR3 mutations in superficial papillary bladder tumors.
64. The R248C mutation appears to be a hot spot for FGFR3 mutations in epidermal nevi.

65. FGFR3 gene mutation is found in thanatophoric dysplasia type 1 and bilateral renal dysplasia.
66. Data indicate that after endocytosis, fibroblast growth factor receptor (FGFR) its bound ligand, FGF1, are sorted mainly to the recycling compartment, while FGFR1-3 with ligand are sorted mainly to degradation in the lysosomes.
67. For the first time in humans, the expression of basic fibroblast growth factor (bFGF) and its receptors FGFR-2, FGFR-3, and FGFR-4 has been documented in ovaries of second- and third-trimester fetuses.
68. Activating mutations of FGFR3 are associated with benign skin tumors.
69. Mutation in the FGFR3 is associated with progression of oral squamous cell carcinoma.
70. Patients with TWIST gene mutations may have more ophthalmic abnormalities including more strabismus, ptosis, NLD, astigmatism, vertical deviations, amblyopia compared with patients with FGFR3 gene mutations.
71. The FGFR3-associated coronal synostosis syndrome (Muenke craniosynostosis) caused by a point mutation (C749G) on the FGFR3 gene resulting in a Pro2 substitution.
72. IGF-1 prevents the apoptosis induced by FGFR3 mutation through the PI3K pathway and MAPK pathway.
73. FGFR3 mutation status and loss of 9q is associated with early-stage bladder carcinomas.
74. The present studies show that MUC1 associates with FGFR3.
75. Double mutation in FGFR3 encoding GLY380LYS is responsible for hypochondroplasia.
76. Findings indicate that: (1) FGFR3 mutations occur in mosaicism and can cause epidermal nevi and (2) other genes are involved in epidermal nevi.
77. The cell model will be useful for the study of FGFR3 function in cartilage and future therapeutic approaches in chondrodysplasias.
78. Distribution in normal endocrine cells and related tumors of the gastroenteropancreatic system; immunoreactive in duodenal G cells.
79. Mutations in growth factor receptor 3 are associated with the pathogenesis of urothelial cell carcinoma.
80. Fibroblast growth factor receptor 3 has a role in trafficking and signaling.
81. Over-expression of FGFR3 may play an important role in liver carcinogenesis.
82. Fibroblast growth factor receptor 3 mutations have a role in development of bladder cancer.
83. FGFR3 mutations do not seem to play a role in bladder cancer progression.
84. We identified a novel ETV6 partner gene, fibroblast growth factor receptor 3 (FGFR3), in a patient with peripheral T-cell lymphoma (PTCL) with a t(4;12).

(p16;p13) translocation.

- 85.FGFR3 and Tp53 mutations do not appear to be associated with progressior
T1G3 transitional bladder carcinomas
- 86.A child who has hypochondroplasia due to an N540K mutation and who has
temporal lobe dysgenesis.
- 87.the importance of the immature FGFR3 proteins as mediators of an abnorm
signaling in thanatophoric dysplasia type II
- 88.FGFR3 mutations were associated with low-stage, low-grade urothelial carc
of the blader.
- 89.strong correlation between mutations of FGFR3 and disturbances of skeletal
REVIEW
- 90.fibroblast growth factor receptor 3 activation is regulated by cytoplasmic ty
kinase Pyk2
- 91.The detection of FGFR3 mutations in FUH (Flat Urothelial Hyperpalsias) sup
the role of this lesion as precursor of papillary bladder cancer.
- 92.These results suggest that intracellular domain mutations define a distinct i
by which mutated FGFR3 could disrupt bone development.
- 93.alternative splicing of FGFR3IIIb results in a secreted isoform that inhibits f
induced proliferation
- 94.interacts with adapter protein SH2-B, and has a role in STAT5 activation

Interactions

Description				
Product	Interactant	Other Gene	Complex Source	Pubs
NP_000133.1	NP_067007.3	C6orf47	HPRD	Pu
NP_000133.1	Fibroblast growth factor 1	FGF1	HPRD	Pu
NP_000133.1	Fibroblast growth factor 8	FGF8	HPRD	Pu
NP_000133.1	Fibroblast growth factor 9	FGF9	HPRD	Pu
NP_000133.1	NP_002077.1	GBR2	HPRD	Pu

General gene information

Markers

W1-15208(e-PCR)

Links: UniSTS:34762

Alternate names: EST318764; RH59111

G15851(e-PCR)

Links: UniSTS:43116

Alternate names: CHLC.UTR_02040_M64347; CHLC.UTR_02040_M64347.P56111

RH18137(e-PCR)

Links: UniSTS:91412

GDB:187013(e-PCR)

Links: UniSTS:155533

GDB:454672(e-PCR)

Links: UniSTS:157443

GDB:454675(e-PCR)

Links: UniSTS:157444

GDB:581559(e-PCR)

Links: UniSTS:157858

GDB:585477(e-PCR)

Links: UniSTS:157890

GDB:881581(e-PCR)

Links: UniSTS:158627

Genotypes

See FGFR3 SNP GeneView Report

See FGFR3 SNP Genotype Report

Phenotypes

Achondroplasia

MIM: 100800

Bladder cancer

MIM: 109800

CATSHL syndrome

MIM: 610474

Cervical cancer, somatic

MIM: 603956

Colorectal cancer, somatic

MIM: 109800

Crouzon syndrome with acanthosis nigricans

MIM: 134934

Hypochondroplasia

MIM: 146000

LADD syndrome

MIM: 149730

Muenke syndrome

MIM: 602849

Nevus, keratinocytic, nonepidermolytic

MIM: 162900

Thanatophoric dysplasia, types I and II

MIM: 187600

Pathways

KEGG pathway: MAPK signaling pathway

04010

KEGG pathway: Regulation of actin cytoskeleton

04810

Reactome Event: Signaling by FGFR

190236

Homology

Mouse, Rat

Map Viewer

GeneOntology

Provided by

Function	Evidence
ATP binding	IEA
fibroblast growth factor receptor activity	NAS
PubMed 7923141	
identical protein binding	

PubMed 14732692	IPI
nucleotide binding	IEA
protein tyrosine kinase activity	IEA
receptor activity	IEA
transferase activity	IEA

Process	Evidence
JAK-STAT cascade	TAS
PubMed 10918587	
MAPKKK cascade	TAS
PubMed 10918587	
cell growth	NAS
fibroblast growth factor receptor signaling pathway	TAS
PubMed 10918587	
protein amino acid phosphorylation	IEA
sensory perception of sound	IEA
skeletal development	TAS
PubMed 8601314	

Component	Evidence
integral to membrane	IEA
integral to plasma membrane	TAS
PubMed 10918587	
plasma membrane	EXP
PubMed 11294897,16597617	

General protein information

Preferred Names
fibroblast growth factor receptor 3

Names
fibroblast growth factor receptor 3
tyrosine kinase JTK4
hydroxyaryl-protein kinase

NP_000133.1
EC 2.7.10.1
NP_075254.1
EC 2.7.10.1

NCBI Reference Sequences (RefSeq)

RefSeqs maintained independently of Annotated Genomes

These reference sequences exist independently of genome builds.

mRNA and Protein(s)

- 1. NM_000142.3→NP_000133.1 fibroblast growth factor receptor 3 isoform 1 precursor**

<p>Description</p> <p>Source sequence(s)</p> <p>Consensus CDS</p> <p>UniProtKB/ Swiss-Prot</p> <p>Conserved Domains (5) summary</p>	<p>Transcript Variant: This variant (1) is missing alternatively spliced exon 8 but utilizes alternatively spliced exon 9, resulting in isoform (1) with the IIIc-type C-terminal half of the IgIII domain.</p> <p>AB209441,AC016773,BC153824</p> <p>CCDS3353.1</p> <p>P22607</p>
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<p>cd00931</p> <p>Location:151-243</p> <p>Blast Score:204</p>	<p>IGcam; Immunoglobulin domain cell adhesion molecule (cam) subfamily; members are components of neural cell adhesion molecules (N-CAM L1), Fascilin II and the insect immune protein Hemolin. The subfamily also includes receptor domains such as the...</p>
<p>cd05100</p> <p>Location:459-753</p> <p>Blast Score:1597</p>	<p>PTKc_FGFR3; PTKc_FGFR3: Protein Tyrosine Kinase (PTK) family; Fibroblast Growth Factor Receptor 3 (FGFR3); catalytic (c) domain. The PTKc family is part of a larger superfamily that includes the catalytic domains of other kinases such as protein serine/threonine...</p>
<p>pfam07714</p> <p>Location:472-748</p> <p>Blast Score:967</p>	<p>Kinase_Tyr; Protein tyrosine kinase.</p>
<p>cl00093</p> <p>Location:253-346</p> <p>Blast Score:132</p> <p>Location:53-110</p> <p>Blast Score:103</p>	<p>IG; Immunoglobulin domain family; members are components of immunoglobulins, neuroglia, cell surface glycoproteins, such as, T-cell receptors, CD2, CD4, CD8, and membrane glycoproteins, such as, butyrophilin and chondroitin sulfate proteoglycan core...</p>
- 2. NM_022965.2→NP_075254.1 fibroblast growth factor receptor 3 isoform 2 precursor**

<p>Description</p> <p>Source sequence(s)</p> <p>Consensus CDS</p> <p>Conserved Domains (4) summary</p>	<p>Transcript Variant: This variant (2) does not contain alternatively spliced exons 8 or 9, resulting in a loss of the C-terminal half of the IgIII domain. In addition, this variant is missing alternatively spliced exon 10 which encodes the transmembrane region, suggesting a soluble receptor.</p> <p>AB209441,AC016773,AF245114</p> <p>CCDS3354.1</p>
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<p>cd00931</p> <p>Location:151-243</p> <p>Blast Score:203</p>	<p>IGcam; Immunoglobulin domain cell adhesion molecule (cam) subfamily; members are components of neural cell adhesion molecules (N-CAM L1), Fascilin II and the insect immune protein Hemolin. The subfamily also includes receptor domains such as the...</p>
<p>pfam07714</p> <p>Location:380-636</p> <p>Blast Score:964</p>	<p>Kinase_Tyr; Protein tyrosine kinase.</p>
<p>cl00093</p> <p>Location:53-110</p>	<p>IG; Immunoglobulin domain family; members are components of immunoglobulins, neuroglia, cell</p>

RefSeqs of Annotated Genomes: Build 36.3

The following sections contain reference sequences that belong to a specific genome build.

Reference assembly

Genomic

1. NC_000004.10 Reference assembly

Range	1765421..1780396
Download	GenBank FASTA Sequence Viewer (beta)

2. NT_006081.18

Range	301275..316250
Download	GenBank FASTA Sequence Viewer (beta)

Alternate assembly (based on Celera assembly)

Genomic

1. AC_000047.1 Alternate assembly (based on Celera assembly)

Range	1708138..1723112
Download	GenBank FASTA Sequence Viewer (beta)

2. NW_921918.1

Range	1708138..1723112
Download	GenBank FASTA Sequence Viewer (beta)

Alternate assembly (based on HuRef)

Genomic

1. AC_000136.1 Alternate assembly (based on HuRef)

Range	1753471..1738498, complement
Download	GenBank FASTA Sequence Viewer (beta)

2. NW_001838896.2

Range	2015637..2000664, complement
Download	GenBank FASTA Sequence Viewer (beta)

Related Sequences

Nucleotide

Protein

Genomic	AC016773.8 (170070..185045)	None
Genomic	AF487554.1	AAM22078.1
		AAM22079.1
Genomic	AY768549.1	AAU89726.1
Genomic	CH471131.2	EAU82562.1
		EAU82563.1
		EAU82564.1
		EAU82565.1
		EAU82566.1
		EAU82567.1
		EAU82568.1
Genomic	S76733.1	AAB33323.1
Genomic	U22410.1	AAA67781.1
mRNA	AB209441.1	BAD92678.1
mRNA	AF238374.1	AAF97749.1
mRNA	AF245114.1	AAF63380.1
mRNA	AF369211.1	AAK54727.1
mRNA	AF369212.1	AAK54728.1
mRNA	AF369213.1	AAK54729.1
mRNA	BC121175.2	AAI21176.1
mRNA	BC128610.1	AAI28611.1
mRNA	BC153824.1	AAI53825.1
mRNA	M58051.1	AAA52450.1
mRNA	M59374.1	AAA63209.1
mRNA	M64347.1	AAA58470.1
mRNA	X84939.1	CAA59334.1
Synthetic	BC166684.1	AAI66684.1

Protein Accession	Links	
P22607.1	GenPept	UniProtKB/Swiss-Prot
Q01J44	GenPept	UniProtKB/TrEMBL
Q59FL9	GenPept	UniProtKB/TrEMBL
Q8NI15	GenPept	UniProtKB/TrEMBL
Q8NI16	GenPept	UniProtKB/TrEMBL
Q96T34	GenPept	UniProtKB/TrEMBL
Q96T35	GenPept	UniProtKB/TrEMBL
Q96T36	GenPept	UniProtKB/TrEMBL
Q9NRB6	GenPept	UniProtKB/TrEMBL

Additional Links

- MIM 134934
- GeneTests for MIM: 100800
- GeneTests for MIM: 134934
- HPRD 00624
- UniGene Hs.1420

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